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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/880,688	POUSTKA ET AL.	
	Examiner	Art Unit	
	TERESA WESSENDORF	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56-60, 66-71, 75, 78-82 and 84-87* is/are pending in the application.

4a) Of the above claim(s) *68, 85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56-60, 66-67, 69-71, 75, 78-82, 84 and 86-87* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 56-60, 66-71, 75, 78-82 and 84-87 are currently pending.

Claims 68 and 85 are drawn to non-elected species and/or inventions and thus this claims remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), there being no allowable generic claim.

Claims 1-55, 61-65, 72-74, 76-77 and 83 have been cancelled.

Claims 56-60, 66-67, 69-71, 75, 78-82, 84 and 86-87 as amended and newly added, are examined on the merits.

Withdrawn Objections/Rejections

In view of the amendments to the claims and applicants' arguments the 35 USC 112, first paragraph (new matter), second paragraph (n part) and 35 USC 102 rejections are withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Amended claims 56-60, 66-67, 69-71, 75, 78-82, 84, 86 and new claim 87, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in

the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

New Matter Rejection

Amended claim 75, which recites the following: "embedding of monomers within a solvent"; "changing the transports units from a solid state of aggregation to a liquid state of aggregation" and "electrostatically charging in claim 87 are not supported in the as-filed specification. MPEP 714.02 clearly states that applicants point out where in the specification support for the newly added limitations appear.

Claim Rejections - 35 USC § 112, second paragraph

Amended claims 56-60, 66-67, 69-71, 75, 78-82, 84, 86 and new claim 87, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record, only for the maintained rejections.

2. Claim 75 is indefinite as to what constitute a "matrix" within the claimed context, especially in the absence of positive definition in the specification. What is the differentiating feature of a matrix from the support?

Response to Arguments

Applicants state that since claim 1 has been cancelled, it is not understood as to what the rejection meant.

In response, the inadvertent rejection of claim 1 is regretted. The rejection refers to independent claim 75.

Applicant states that claim 75 has amended the description to refer to the definition of FIG. 25 in which the matrix is schematically seen. The numeral listing also includes the term matrix. "Matrix" is for example defined among others as "a mass by which something is enclosed or embedded". See Webster Third New International Dictionary. Here the matrix included the solvent as now recited in the claim. The support is where the monomers are being coupled to after the mobilization step.

In reply, there is no Fig. 25 in the instant specification. The definition of a matrix is not controverted. The issue is the matrix as claim which is not positively recited in the specification.

5. Claim 67 is unclear as to what would constitute “preliminary stages” of D or L amino acids. This rejection has similar import to claim 69.

Response to Arguments

Applicants state that the rejection is moot with the amendments to the claim.

In reply, the term "preliminary" is still present in claim 69.

Claims 56-60, 66-67, 69-71, 75, 78-82, 84 and 86-87 as amended and newly added are rejected under 35 USC 112, as follows:

A. Claim 75 is being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: changing the transport units from a solid to a liquid state of aggregation. It is not clear whether simply mobilizing and diffusing the monomers changed the transport units from a solid to a liquid state of aggregation.

B. Claim 75 is unclear with the amendment cancelling "matrix". It is unclear how a monomer is embedded in a liquid that is in a solid state of aggregation.

C. Claims 75 and 80 are unclear as to the washing away of the transport units. Are these different from the non-linked monomers? (Cf. with new claim 87).

D. The term "defined" in claims 75, 80 and “suitable” in claim 87 are relative terms which render the claim indefinite. The terms are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear how the monomers are considered to be “defined” in a position. Also it is unclear and indefinite as to the manner or the kind of amino acid or nucleic acid that are considered to be suitable for solid phase synthesis.

E. Claim 87 is unclear as to the essentiality of “electrostatically charging” the transport units. Does the laser printing would not operate without first electrostatically charging the transport units?

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejection - 35 USC § 103

Claims 54, 56-60, 66-67, 69-71, 75, 77-82, 84 and 86, as amended, are rejected under 35 U.S.C. 103(a) as being obvious over Zebala (USP 6951682).

Zebala throughout the patent discloses at e.g., col. 4, lines 14-62:

> …..[M]ethods for making a coated article comprising a substrate and at least two separate porous coatings, comprising the steps of: (a) applying to a substrate a substantially uniform layer of a solution comprising metal oxide particles dispersed in a volatile liquid; (b) evaporating the volatile liquid from the layer, forming a gelled network of metal oxide particles on the substrate, wherein the gelled network forms a porous coating ranging from 0.05 to 25 microns thick; (c) covering the porous coating with a layer of photoresist comprising a base soluble component; (d) irradiating the photoresist, such that a first region of photoresist is rendered substantially removable with an aqueous alkaline developer, and such that a second region is not so removable; (e) contacting at least the first region with an aqueous alkaline developer to remove at least the first region of photoresist and porous coating underlying the first region, without substantially removing the second region of photoresist or porous coating underlying the second region; (f) removing remaining photoresist with an organic solvent, resulting in separate porous coatings on discrete regions of the substrate; and (g) attaching one or more compounds to each of the separate porous coatings. The solution may further comprise extended polymers of a substantially hydrolyzed metal alkoxide linked to the metal oxide particles, wherein the weight ratio of metal oxide particles to the substantially hydrolyzed metal alkoxide ranges from 1 to 1000. Optionally, prior to the step of attaching two or more compounds, the porous coating is cured at a temperature and for a time sufficient to increase the porous coating strength

Zebala discloses at e.g., col.8, line 43 up to col. 29,line 3:

> A compound is said to be "attached" to a substrate surface if the compound substantially remains on the surface during photoresist application and removal (i.e., at least 60% of the attached compounds are not removed when such processes are performed as described). The percentage of compounds removed under particular conditions may be readily determined using labeled molecules, and monitoring the loss of label during photoresist application and removal. Attachment may be covalent or non-covalent. Noncovalent interactions that may be employed include, for example,

electrostatic interactions…, and magnetism. In some embodiments, a mixture of covalent and noncovalent interactions may be used. Suitable magnetizing agents for use in a magnetic field include paramagnetic lanthanide ions such as erbium, dysprosium, holmium, thulium, and gadolinium…… Alternatively, micron-scale and smaller magnetic affinity particles may be used such as magnetite, and magnetic porous glass……

"Gelled network" refers to an aggregation of particles linked together to form a porous three-dimensional network. Particles may be linked covalently or noncovalently through the use of a polymeric binder. Alternatively, particles may be linked covalently or noncovalently without the use of a binder, through interactions of chemical groups on the surface of the particles…. and photoinduced linkages using, for example, a bis-azide…..The extent of linking sufficient to constitute a "gelled network" will be such that less than 20%, and more preferably less than 5%, of the network is lost after contact with any process agent (e.g., irradiation, photoresist, developers, strippers and reagents). Accordingly, the extent of linking required will depend on the exact nature of the process agents. For example, photoresists that exhibit higher degrees of swelling will require gelled networks with higher degrees of linking so as to balance the forces of swelling and prevent physical disruption of the gelled network. The percent loss of the network after contact with process agents can be readily assessed using nitrogen adsorption isotherms and the Brunauer-Emmett-Teller (BET) method. The BET method allows the surface area of the gelled network to be accurately measured, and the percent change in surface area after contact with a process agent will be equivalent to the percent loss of the gelled network. Other methods for assessing the percent loss of the gelled network after contact with process agents will be apparent to one of ordinary skill in the art.

"Hybridization" refers to the base-pairing or aggregation of one nucleobase polymer to another nucleobase polymer via complementary regions. The polymers may be, for example, DNA, PNA, morpholino-based nucleobase polymers and/or other nucleobase polymers. Such base-pairing or aggregation should be detectable using standard assays (e.g., detection

of a marker linked to one nucleobase polymer). Whether or not a particular nucleobase polymer remains base-paired or aggregated with a target nucleobase polymer depends on the degree of complementarity, the length of the aggregated elements, and the stringency of the binding conditions. At a higher stringency, hybridization requires a higher degree of complementarity or length

"Irradiation" refers to the application of radiation to a target. The amount of irradiation depends on the desired result of the irradiation. In general, irradiation is sufficient to achieve a desired chemical modification on an irradiated molecule. For example, irradiation of a positive photoresist layer is sufficient to permit substantial removal of photoresist from irradiated regions.

"Mask" refers to a substantially transparent support material with substantially opaque regions in a precise pattern where it is desired that light be blocked when one side of the mask is illuminated. In some embodiments the substantially opaque regions are derived through a photographic process using a photoplotting device (e.g., as in masks commonly used in printed circuit board manufacturing). In other embodiments the mask is derived from a substantially transparent support material coated with a substantially opaque material which is photoablated by a narrowly focused laser producing precisely defined transparent regions (e.g., chrome on glass masks).

"Photoresist" refers to a material that, upon irradiation, sustains a chemical reaction that allows irradiated and non-irradiated regions to be separated from one another. Although the separation may be simultaneous with the irradiation step (e.g., in laser ablation), it often requires an additional process step or steps (e.g., exposure to a developer). The chemical reaction may involve the formation or breakage of chemical bonds with such bond changes occurring in either an intramolecular or intermolecular fashion. In most applications, a photoresist is applied to a flat surface as a relatively thin liquid layer and evaporated. A "negative photoresist" refers to a photoresist that leaves photoresist on the surface in irradiated regions, while a "positive photoresist" refers to a photoresist that leaves photoresist on the surface in regions that were not irradiated.

As alternatives to the use of masks, other methods may be used to illuminate selected regions of photoresist. For example, the substrate may be translated under a modulated laser or diode light source (see Feyrer et al., U.S. Pat. No. 4,719,615). In alternative embodiments, a laser galvanometric scanner may be utilized. In other embodiments, the irradiation of the photoresist may take place on or in contact with a fiber optic light source, or a liquid crystal. By appropriately modulating liquid crystals, light may be selectively controlled so as to permit light to contact selected regions of the photoresist. Such a liquid crystal is also referred to as a "programmable mask," or an integrated circuit spatial light modulator (ICSLM), manufactured by Displaytech (Boulder, Colo.). Alternatively, irrad…. light will be directed to extremely small regions, being limited by diffraction to a size directly proportional to the wavelength of light. In order to mask illumination to regions smaller than a wavelength of light, more elaborate techniques may be utilized. For example, light may be directed at the photoresist by way of molecular microcrystals on the tip of, for example, micropipettes After the irradiating step is completed, the photoresist is contacted with developer. This results in the selective, substantial removal of photoresist, and underlying porous coating, from irradiated (positive photoresists) or non-irradiated (negative photoresists) regions, leaving only photoresist and porous coating in discrete regions (see FIG. 1C, illustrating the process for a positive photoresist). The developer is selected based upon the type of photoresist. For photoresists comprising a base soluble (e.g., phenolic polymer) component, the developer preferably has an alkaline pH, more preferably 9 to 12 pH units…. The rate of photoresist dissolution can be increased by increasing the pH or increasing the temperature, limited mainly by solubility considerations of remaining photoresist….. irradiated photoresist is contacted with developer at a temperature from 20.degree. C. to 30.degree. C., and most preferably at a temperature from 23.degree. C. to 27.degree. C., for sufficient time to effect substantial removal of desired regions of the irradiated photoresist and underlying porous coating.

In the absence of photoresist, the use of an alkaline developer results in no detectable dissolution of the porous coating. It was unexpectedly found, within the context of the present invention, that dissolution of irradiated photoresist results in the dissolution of the underlying porous coating. Although the actual mechanism is uncertain, it is known that the phenomenon is mitigated and even abolished by subjecting the porous coating to temperatures normally associated with high temperature curing. Presumably, the formation of oxane bonds during high temperature curing strengthens the porous coating against the putative forces that develop during the photopatterning process. Accordingly, it is necessary to avoid prolonged exposure to temperatures greater than about 100.degree. C. until after the porous coating is patterned.

For photoresists not comprising a phenolic polymer, other developers (e.g., etchants) may be used to arrive at a patterned porous coating disclosed herein…… Suitable etchants for use in combination with alternative photoresists will be familiar to those skilled in the art….

After treatment with developer, remaining photoresist is removed by contact with a stripping solution. The stripping solution is generally an organic solvent that selectively dissolves the photoresist, leaving only the patterned porous coating. In embodiments employing a phenolic polymer, the stripping solution may be, for example, a ……. isopropanol, …..acetate, or any of a wide number of organic solvents well known in the art….

In some embodiments, each Gn group is selected from 1 of 10 different compositions. By forming every Gn combination, 10.sup.4 or 10,000 analogues are synthesized in a total of 40 cycles. Accordingly, it will be appreciated by those of skill in the art that the above method can be used for the parallel production of supports bearing thousands or millions of drug candidates and other compounds using barrier layers and the photolithographic techniques disclosed herein.

Claims 56-60 and 78-79 drawn to the claim temperature would be obvious in view of the disclosure of Zabala that the temperature should be less than 100.

Response to Arguments

Zebala describes a lithographic method of the type that provides a specialized solid support which is meant to have a large accessible surface in the lithographic method. Zebala does not use laser printing.

In reply, attention is directed to Zebala's disclosure above which states:

> ….For example, the substrate may be translated under a modulated laser or diode light source (see Feyrer et al., U.S. Pat. No. 4,719,615).
>
> Attention is further directed to col. 37, lines 37-52 which recites:
>
> Arrays of ligands may be attached to the porous coating using any placement method that is compatible with the synthesis of compounds on a porous three dimensional object including, for example, **ink-jet technology** (see Brennan, U.S. Pat. No. 5,474,796). Most preferably, however, ligand arrays are formed on the porous support using methods and compositions described more fully in co-pending Application Ser. No. 09/326,479 entitled, "Methods and Compositions For Performing an Array of Chemical Reactions on a Support Surface" and U.S. Pat. No. 6,569,598, entitled "Solvent-Resistant Photosensitive Compositions." Synthesis methods employing photoremovable groups are not generally compatible with the porous coatings described herein, as a result of incomplete photodeprotection, and such techniques should generally be avoided.

Accordingly, Zebala's disclosure of linking method using ink-jet technology which is cited only as an example and teaching of laser would lead one having ordinary skill in the art to laser printing. Read in the light of the specification, laser or ink-jet technology is known in the art to attach monomers to surfaces.

Applicants argue that the claims recite that at the end the non-linking molecules are being washed away. This not the case with Zebala, where all molecules remain on the surface and no transport units nor non-linked monomers are being removed, let alone being washed away. Zebala explicitly fortifies the multilayered particles to get a stable support, see col. 11, lines 20 to 65 (gelled network).

In reply, attention is drawn to Zebala’s disclosure above which states:

> After treatment with developer, remaining photoresist is removed by contact with a stripping solution.

New claim 87 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zebala et al in view of Suzuki (USP 5581337) for reasons of record as reiterated below. Zebala is discussed above. Zebala does not disclose a method wherein the monomers are electrically charged.

Suzuki discloses at e.g., col. 6, lines 5-35 said electrical charged resulting in electrostatic image.

Accordingly, to electrically charge the monomers would have been obvious to one having ordinary skill in the art at the time the invention was made. There is a reasonable expectation of success to electrically charge the transport units as successfully done in the art as taught by Suzuki, supra.

Response to Arguments

Applicants state that claim 83 has been cancelled and hence the rejection is moot.

In response, new claim 87 replaced claim 83. Hence, the rejection is maintained.

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

This application contains claims 68 and 85 drawn to nonelected invention. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA WESSENDORF whose telephone number is (571)272-0812. The examiner can normally be reached on flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/TERESA WESSENDORF/
Primary Examiner, Art Unit 1639